

bottom edge 2190B" rather than "second bottom edge 250B". Applicant has amended the specification (paragraph beginning on page 45, line 17) to make the specification reference numeral 250B consistent with the reference numeral 250B in Fig. 34.

Regarding the drawing objections listed in paragraph 3 of the last office action, applicant is enclosing a corrected Fig. 15A that changes reference numeral 162 to reference numeral 163 to be consistent with the specification and that deletes reference numeral 164B from the drawing. Applicant is also enclosing a corrected Fig. 15B that deletes reference numerals 164B and 166 from the drawing. Reference numeral 164A should be in Fig. 15B, and applicant has amended the specification paragraph beginning on page 30, line 17 to include reference to valve actuator 164A. Applicant is also enclosing a corrected Fig. 21 that deletes reference numeral 56 from the drawing. Regarding the Examiner's objection to reference numerals 53 and 56 in Fig. 22, applicant respectfully submits that these reference numerals are mentioned in the specification with regards to Fig. 22 on page 26, lines 20-26.

Regarding the three drawing objections listed in paragraph 4 of the last office action, the drawings are actually labeled with the correct reference numerals but the applicant made several typographical errors in the specification when typing the reference numerals. The specification has been amended to fix these problems.

Claims 1-21 are canceled and claims 22-42 are added. No new matter has been introduced.

Applicant believes claims 22-42 comply with 35 U.S.C. § 112. There is now antecedent basis for each claim element.

Applicant is submitting a terminal disclaimer to overcome the provisional double-patenting rejection with regard to copending application Ser. No. 09/194,374.

Claims 1-4, 6-15, and 17-21 stand rejected under 35 U.S.C. § 102(b) as anticipated by Ulmer (U.S. Patent 5,674,743). Claims 5 and 16 stand rejected under 35 U.S.C. § 103(a) as being obvious over Ulmer. Applicant requests reconsideration of these rejections, as now applicable to claims 22-42, in view of the following arguments.

Claims 22-33

Applicant respectfully submits that independent claim 22 is novel and patentable over Ulmer because, for instance, Ulmer does not disclose or suggest a reaction vessel having an inlet port connected to a reaction chamber via an inlet channel and having an outlet port connected to the reaction chamber via an outlet channel, wherein the inlet port of the vessel is connected to the first channel in the body and wherein the outlet port of the vessel is connected to the second channel in the body.

In Ulmer, a sample cell 500 has a single microchannel 75. Ulmer does not disclose or suggest the structure recited by the applicants.

For at least the foregoing reasons, claim 22 and claims 23-33 depending therefrom are patentable.

Claims 34-42

Applicant respectfully submits that independent claim 34 is novel and patentable over Ulmer because, for instance, Ulmer does not disclose or suggest at least one polymeric film attached to a rigid frame to form a major wall of a reaction chamber.

Ulmer discloses a very different structure, in particular a sample cell in which three sheets of glass are employed, a microchannel being etched between the two bottom sheets, and a refrigeration system being etched in the upper sheet. Ulmer does not disclose or suggest at least one polymeric film attached to a rigid frame to form a major wall of a reaction chamber.

For at least the foregoing reasons, claim 34 and claims 35-42 depending therefrom are patentable.

CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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PATENT

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-752-2469.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE SPECIFICATION**

Please replace the paragraph beginning on page 29, line 31 with the following paragraph:

Fig. 25 shows another vessel 206 designed to be used in a horizontal orientation. The vessel 206 has an inlet port 41 and an inlet channel 50 connecting the inlet port 41 to the bottom of the chamber 42. The vessel also has an outlet port 43 and an outlet channel [50] 52 connecting the outlet port 43 to the top of the chamber 42. Thus, any air bubbles in the chamber 42 may escape through the outlet channel 52 without becoming trapped. Fig. 26 shows another vessel 207 having two inlet ports 41, 45 and one outlet port 43. Inlet channels 50, 54 connect the respective inlet ports 41, 45 to the chamber 42, and outlet channel 52 connects the chamber 42 to outlet port 43. Many other different embodiments of the vessel are also possible. In each embodiment, it is desirable to evacuate the chamber 42 from the highest point (with respect to gravity) in the chamber and to introduce liquid into the chamber from a lower point.

Please replace the paragraph beginning on page 30, line 17 with the following paragraph:

Figs. 15A-15B illustrate two types of valves used in the cartridge. As shown in Fig. 15A, there are two types of fundamental concepts to the valve action, and hence two types of valves. The first valve uses a cone-shaped or conical valve seat 160 formed in the middle cartridge piece 24. The valve seat 160 is a depression, recess, or cavity molded or machined in the middle piece 24. The valve seat 160 is in fluid communication with a chamber 167 through a port or channel 157 that intersects the center of the conical valve seat 160. As shown in Fig. 15B, a valve actuator [164] 164A having a spherical surface is forced against the elastic membrane 63 and into the valve seat 160, establishing a circular ring of contact between the membrane 63 and the valve seat 160. The kinematic principle is that of a ball seated into a cone. The circular seal formed by the membrane 63 and valve seat 160 prevents flow between the channel 157

(and hence the chamber 167) and a side channel 158 extending from a side of the valve seat 160. The side channel 158 is defined by the membrane 63 and the middle cartridge piece 24.

Please replace the paragraph beginning on page 34, line 29 with the following paragraph:

A conical valve seat 160 (previously described with reference to Figs. 15A-15B) is formed in the middle cartridge piece 24 below the chamber 414 to control the flow of liquid between the chamber 414 and a connecting channel 411. The valve is opened and closed by a valve actuator [188] 186 having a flange 187 and a spring 188 pressing against the flange 187 to hold the valve closed until a downward force is applied to the actuator 186. The downward force is preferably supplied by a solenoid that pulls down the actuator 186 to open the valve. The valve actuator 186 and solenoid are preferably located in the instrument.

Please replace the paragraph beginning on page 45 line 17 with the following paragraph:

--Fig. 34 shows a partially cut-away, isometric view of the chamber of the vessel inserted between the plates 190A, 190B (the top portion of the vessel is cut away). The vessel preferably has an angled bottom portion (e.g., triangular) formed by the optically transmissive side walls 57A, 57B. Each of the plates 190A, 190B has a correspondingly shaped bottom portion. The bottom portion of the first plate 190A has a first bottom edge 250A and a second bottom edge [2190B] 250B. Similarly, the bottom portion of the second plate 190B has a first bottom edge 252A and a second bottom edge 252B. The first and second bottom edges of each plate are preferably angularly offset from each other by the same angle that the side walls 57A, 57B are offset from each other (e.g., 90°). Additionally, the plates 190A, 190B are preferably positioned to receive the chamber of the vessel between them such that the first side wall 57A is positioned substantially adjacent and parallel to each of the first bottom edges 250A, 252A and such that the second side wall 57B is positioned substantially adjacent and parallel to each of the second bottom edges [2190B] 250B, 252B. This arrangement provides for easy

optical access to the optically transmissive side walls 57A, 57B and hence to the chamber of the vessel. A gel or fluid may optionally be used to establish or improve optical communication between each optics assembly and the side walls 57A, 57B. The gel or fluid should have a refractive index close to the refractive indexes of the elements that it is coupling.--

Please replace the paragraph beginning on page 59 line 30 with the following paragraph:

Following priming, valve 115 and pressure port 116 are closed and valves 107 and 114 are opened. At the same time, a pressure of 20 psi is applied to the sample chamber 65 through the pressure port 105 for about 15 seconds to force the sample to flow through the channel 106, through the filter stack 87 in the chamber [87] 86, through the channels 110, 111, 112 and into the vented waste chamber 68. As the sample passes the detection region 136 in the channel 106, the reflective optical sensor 144 (Fig. 13) may be used to determine when the sample chamber 65 has been emptied. As the sample liquid flows through the filter stack 87, target cells or viruses in the sample are captured. When a predetermined volume of sample reaches the waste chamber 68, some of the liquid spills over into the sensor chamber 120, triggering the next step in the protocol. Alternatively, instead of using feedback from optical sensors to trigger events, the steps in a predetermined protocol may simply be timed, e.g., applying predetermined pressures for predetermined durations of time to move known volumes of fluid at known flow rates.

IN THE CLAIMS:

Please cancel claims 1-21 and replace with claims 22-42 as follows:

22. A device for conducting a chemical reaction, the device comprising:
- a) a body having at least first and second channels formed therein; and
  - b) a reaction vessel extending from the body, the reaction vessel having:
    - i) a reaction chamber;

- ii) an inlet port connected to the reaction chamber via an inlet channel; and
- iii) an outlet port connected to the reaction chamber via an outlet channel;

wherein the inlet port of the vessel is connected to the first channel in the body and wherein the outlet port of the vessel is connected to the second channel in the body.

- 23. The device of claim 22, wherein the body further includes a vent in fluid communication with the second channel for venting gas from the second channel.
- 24. The device of claim 22, further comprising a differential pressure source for forcing fluid in the first channel in the body to flow through the inlet port of the vessel and into the reaction chamber.
- 25. The device of claim 22, wherein the vessel includes:
  - i) a rigid frame defining side walls of the reaction chamber; and
  - ii) first and second polymeric films attached to opposite sides of the rigid frame to form opposing major walls of the reaction chamber.
- 26. The device of claim 25, wherein each of the major walls is sufficiently flexible to conform to a respective thermal surface.
- 27. The device of claim 25, wherein at least two of the side walls are optically transmissive and angularly offset from each other.
- 28. The device of claim 22, wherein the ratio of the width of the chamber to the thickness of the chamber is at least 4:1, and wherein the chamber has a thickness less than 2 mm.

29. The device of claim 22, wherein the body further includes a mixing chamber for mixing a fluid sample with amplification reagents, the mixing chamber being connected to the inlet port of the vessel via the first channel.
30. The device of claim 22, wherein the body has formed therein:
  - i) a sample flow path; and
  - ii) a separation region in the sample flow path for separating a desired analyte from a fluid sample, the separation region being connected to the inlet port of the vessel via the first channel.
31. The device of claim 30, wherein the separation region in the body comprises:
  - a) a lysing chamber in the sample flow path for lysing cells or viruses in the sample to release material therefrom; and
  - b) at least one solid support positioned in the lysing chamber for capturing the cells or viruses to be lysed.
32. The device of claim 22, wherein the vessel includes a plurality of walls defining the reaction chamber, at least one of the walls comprising a flexible sheet or film, and the device further comprises:
  - a) at least one thermal surface for contacting the sheet or film;
  - b) means for increasing the pressure in the reaction chamber, wherein the pressure increase in the chamber is sufficient to force the sheet or film to conform to the thermal surface; and
  - c) at least one thermal element for heating or cooling the surface to induce a temperature change within the chamber.
33. The device of claim 1, wherein the vessel includes two opposing major walls and sidewalls connecting the major walls to each other to form the reaction chamber,



at least two of the side walls are optically transmissive and angularly offset from each other, and the device further comprises an optics system having at least one light source for transmitting light to the reaction chamber through a first one of the optically transmissive side walls and having at least one detector for detecting light emitted from the chamber through a second one of the optically transmissive side walls.

34. A device for conducting a chemical reaction, the device comprising:
- a) a body having at least one flow path formed therein; and
  - b) a reaction vessel extending from the body, the vessel comprising:
    - i) a rigid frame defining side walls of a reaction chamber;
    - ii) at least one polymeric film attached to the rigid frame to form a major wall of the reaction chamber; and
    - iii) an inlet port for adding fluid to the reaction chamber;
- wherein the inlet port of the vessel is connected to the at least one flow path in the body.
35. The device of claim 34, wherein the vessel includes first and second flexible sheets attached to opposite sides of the rigid frame to form two opposing major walls of the reaction chamber.
36. The device of claim 34, wherein the major wall is sufficiently flexible to conform to a thermal surface.
37. The device of claim 34, wherein at least two of the side walls are optically transmissive and angularly offset from each other by about 90°.

38. The device of claim 34, wherein the ratio of the width of the chamber to the thickness of the chamber is at least 4:1, and wherein the chamber has a thickness in the range of 0.5 to 2 mm.
39. The device of claim 34, wherein the body has formed therein:
- i) a sample flow path;
  - ii) a separation region in the sample flow path for separating a desired analyte from a fluid sample; and
  - iii) an analyte flow path connecting the separation region to the inlet port of the vessel.
40. The device of claim 39, wherein the separation region in the body comprises:
- a) a lysing chamber in the sample flow path for lysing cells or viruses in the sample to release material therefrom; and
  - b) at least one solid support positioned in the lysing chamber for capturing the cells or viruses to be lysed.
41. The device of claim 34, further comprising:
- a) at least one thermal surface for contacting the major wall of the reaction chamber;
  - b) means for increasing the pressure in the reaction chamber, wherein the pressure increase in the chamber is sufficient to force the major wall to conform to the thermal surface; and
  - c) at least one thermal element for heating or cooling the surface to induce a temperature change within the chamber.
42. The device of claim 34, wherein at least two of the side walls of the reaction chamber are optically transmissive and angularly offset from each other, and wherein the device further comprises an optics system having at least one light

source for transmitting light to the reaction chamber through a first one of the optically transmissive side walls and having at least one detector for detecting light emitted from the chamber through a second one of the optically transmissive side walls.